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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/545,199	04/06/2000	David E. Lowery	28341/6227.1NCP	9014

7590 05/16/2005

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/545,199	LOWERY ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 7-24 and 31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 7-24,31 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 7-24 and 31 are pending.
Claims 1-6, 25-30 and 32-51 have been canceled.
1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections Withdrawn

1. Claims 7-24 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of Applicant's amendment of claim 14 and remarks.
2. Claims 7-24 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Kooistra et al (1976), in light of Applicant's remarks.

Rejections Maintained

3. Claims 7-24 and 31 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims read on mutations of the polynucleotide of SEQ ID NO: 4, or attenuated bacteria comprising such polynucleotides, and species homologs thereof. However, the specification does not provide adequate written description to support either species homologs to SEQ ID NO: 4, or any mutation resulting in decreased activity of the protein. There is inadequate written description to support claims to attenuated bacteria that comprise species homologues of the disclosed polynucleotide.
4. Claims 7-24 and 31 rejected under 35 U.S.C. 1 12, First paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are described above. The claims are rejected because the applicant has not provided sufficient disclosure in the application to enable one skilled in the art to make or use any mutants of any Pasteurellaceae atpG polynucleotide, or a bacterium comprising such, wherein the mutation results in a decreased activity of a gene product, is maintained for reasons of record and responses set forth below.
5. Claims 7-24 and 31 rejected under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention., is maintained for reasons of record and responses set forth below.

Response to Arguments

6. The rejection of claims 7-24 and 31 under 35 U.S.C. 112, first paragraph (written description), as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention is traversed on the grounds that:

a. "[T]he Applicant's are claiming bacteria and they are claiming said bacteria comprising a mutation in a nucleotide sequence with a specific structure:function relationship in the claims. The Applicant's are not claiming polynucleotide sequences per se."

7. It is the position of the examiner that all of the claims are directed to a highly variable genus of attenuated Pasteurellaceae bacteria, based upon the recitation of the phrase "at least 70% identical to the atpG amino acid sequence of SEQ ID NO 4". While SEQ ID NO 4 is an amino acid sequence encoded by 866 nucleotides, what is being claimed are atpG amino acid sequences encoded by nucleotides that contain from 606 to 1126 nucleotides based upon the recitation of the phrase "70% identical", which would result in an amino acid sequence of 202 to about 372 amino acids. Applicant provides original descriptive support for two atpG amino acids sequence of 288 and 289 amino acids in length. The genus of nucleotide sequences must than be mutated as the claim requires that the nucleotide sequence be mutated to decrease atpG biological activity.

8. In light of the highly variable genus of nucleotide sequences in a Pasteurella bacteria not having been described, and thus the expressed atpG amino acid sequence encoded there by, not having been described, the mutant coding sequences contained in the bacteria for the highly variable genus of nucleotide sequences also has not been described.

Applicant has provided written descriptive support for two species of attenuated bacteria that may have mutations in the nucleotide sequence, specifically SEQ Id NO 3 which encodes

the amino acid sequence of SEQ Id No 4, as well as SEQ Id NO 132. The specification does not provide adequate written description to support species homologs to SEQ ID NO: 4, defined by the combination of claim limitations "at least 70% identical" together with any mutation resulting in decreased activity of the protein. There is inadequate written description to support claims to attenuated bacteria that comprise species homologues of the disclosed polynucleotide.

9. Applicant asserts that they are not claiming polynucleotide homologs and they are not claiming such homologs only by their function.

10. It is the position of the examiner that the claimed invention is directed to a combination composition that comprises a bacteria and a mutant polynucleotide. The polynucleotide in the bacteria is not limited to the coding sequence that encodes the amino acids of SEQ Id NO 4, but includes functional homologs of the polynucleotide that encodes SEQ ID NO 4, based upon the recitation of the phase "70% identical". A polynucleotide that encodes SEQ ID NO 4 may share 66% identity with SEQ ID NO 3, based upon variations in codons for each amino acid, and the starting polynucleotide that is subsequently mutated may share an additional 30% sequence variation which results in a starting polynucleotide of about 46% identity with the coding sequence for SEQ ID NO 4, specifically SEQ ID NO 3.

11. The mutant polynucleotides contained in the bacteria are required to attenuate the claimed bacteria because no other components of the claimed bacteria are required to be changed, and thus must be responsible for the attenuated state of the bacteria. Therefore, the critical component of the claimed combination composition is the polynucleotide, and case law pertaining to DNA inventions is clearly applicable to the instantly claimed invention.

Applicant has not shown possession of the highly variable genus of polynucleotides based upon a disclosure that suggests obtaining bacteria with mutations in an atpG polynucleotide and a method of screening for the mutant bacteria that evidence "decreased atpG biological activity" .

The claimed bacteria comprise the mutant polynucleotide sequence in such a way as to attenuate the bacteria due to the specific mutations introduced into the polynucleotide coding

structure, the mutations being based upon the description of the polynucleotide. Applicant's assertion that case law pertaining to DNA inventions is not applicable to what is being claimed mischaracterizes the critical elements of Applicant's claimed invention. The examiner provided evidence that any mutation in the gamma subunit of ATP synthase of a bacteria does not result in attenuation (see Humbert et al (1989). Humbert et al showed the mutant atpG subunit (gamma subunit) to result in bacterial resistence to antibiotics, which is the opposite of attenuation or weakening of the bacteria to be more susceptible to antibiotics.

12. Applicant in support for the instantly claimed genus states "members of the claimed genus can be identified by these common attributes."

13. It is the position of the examiner, that possession does not require further future identification of members of the genus.

14. Applicant asserts that they "should be permitted to claim as broadly as the art allows and the specification describes and enables." Applicant states the Guidelines only provided 1 species for a sequences having 95% identity and this is permissible.

15. It is the position of the examiner that rejection of the claims was under 35 USC 112, first paragraph that requires possession at the time of filing of what is being claimed. What Applicant has claimed are mutant attenuated bacteria that need only have an atpG polynucleotide that shares 46% sequence identity (SEQ Id No 4 permits 66% sequence identity with SEQ ID NO 3, and then 70% of 66% is equal to 46% sequence identity) with SEQ ID NO 3 (NA). Clearly a sequence which evidences mutations with a reference sequence that only

shares 46% sequence identity to SEQ ID NO 3, is not what is exemplified in the Guidelines to which Applicant refers that permits 95% sequence identity at the nucleotide level. The instant Specification provides original descriptive support for two specific species of bacteria and the corresponding two atpG coding sequences that were mutated . What is claimed is a highly variable genus and Applicant has not described the highly variable in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicant's traversal is not commensurate in scope with the instantly claimed invention.

16. Arguments directed to enablement based on methods of screening (Applicant's remarks, page 9, paragraph 2, "Southern hybridization") to identify potential members of the claimed genus does not show possession of the claimed invention at the time of filing.

17. At page 10, paragraph 2, of Applicant's Remarks, traversal is made that "they do not need to specifically point out where the mutation is located within the atpG sequence, as long as the mutation disrupts the expression or function of the encoded atpG polypeptide."

18. It is the position of the examiner that the claims require "a mutation in a nucleotide sequence that encodes an atpG polypeptide", thus mutations that disrupt expression outside the coding sequence are not encompassed by the claimed invention. Applicant's traversal is not commensurate in scope with the combination of claim limitations recited, at least in independent claim 7. Additionally, prior to mutation of an atpG polynucleotide sequence, Applicant must have possession of the coding sequence. Applicant has not provided a representative number of species for the highly variable genus of mutant bacteria that comprise a mutated atpG

polynucleotide that need only share 46% sequence identity to the coding sequence for SEQ ID NO 4. The lack of written description rejection under 35 USC 112, first paragraph is maintained for reasons of record.

19. The enablement rejection of claims 7-24 and 31 under 35 U.S.C. 1 12, First paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is traversed on the grounds that one of skill in the art would be able to identify and make Pasteurellaceae bacteria comprising variants of the atpG polypeptide without undue experimentation.

20. It is the position of the examiner that the issue raised was not being able to identity Pasteurellaceae bacteria, but where in the coding sequence a mutation could be made to achieve an active atpG polypeptide, but with reduced activity, and how many mutations are permitted to produce an atpG polypeptide with desired characteristics. While those participating in the art of the relevant technology (genetic and protein manipulation) are generally highly skilled, the art is also rife with complexity. Knowledge of the sequence of protein or polynucleotide alone is not sufficient for those skilled in the art to make any mutation to a molecule and have confidence as to the effects that such a mutation would have. Applicant has invited others in the art to determine what mutations would achieve the desired affect without providing them any guidance indicating what the potential operable embodiments are. Given the complexity of the art, the breadth of the claims, the number of potential mutations, and the lack of guidance provided by the applicant, the examiner finds that there is insufficient information in the specification to enable those skilled in the art to practice the claimed invention without undue experimentation.

21. The rejection of claims 7-24 and 31 under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention because the applicant has not described how a mutation in the protein coding regions can result in decreased expression of the gene product has been traversed on the grounds that the "amendment to claim 14 herein renders the rejection moot."

22. It is the position of the examiner that the independent claim 7, from which all other claims directly or indirectly depend, the scope of which is further limited by claim 14 which recites the combination of claim limitations "resulting in decreased atpG polypeptide expression", includes mutations in non-coding regions of a bacterial gene. SEQ Id NO 4 does not include any non-coding regions of a gene that would regulate polypeptide expression. The enablement rejection is maintained for reasons of record; Applicant's amendment of claim 14 to remove the phrase "gene product", has not obviated the scope of enablement rejection. No specific sequences of SEQ ID NO 4 have been identified as being critical to polypeptide expression levels and upon mutation would result in decreased polypeptide expression.

Conclusion

23. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

1. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

2. Swiss-prot accession number P43716 is cited to show the amino acid sequence for Haemophilus influenzae Atpase gamma subunit.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by b telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
May 12, 2005

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